

27 03 185

45-715

Translated from German by
SCIENTIFIC TRANSLATION SERVICES
411 Wyntre Lea Dr.
Bryn Mawr, PA 19010

(51)	Int. Cl. ² :	C 07 C 127/15
(19)	FEDERAL REPUBLIC OF GERMANY	A 61 K 7/00
	GERMAN PATENT OFFICE	A 61 K 7/48
		C 11 D 3/48
(11)	Offenlegungsschrift 27 03 185	
(21)	Reference Number:	P 27 03 185.2
(22)	Filing Date:	January 27, 1977
(43)	Date laid open to public inspection:	August 10, 1978
(30)	Union Priority:	
	(32) (33) (31)	

(54)	Title:	Cosmetic Agents Containing Skin Moisturizers
(71)	Applicant:	Henkel KGaA, 4000 Düsseldorf
(72)	Inventors:	Möller, Dr. Hinrich, Cert. Chem.; Osberghaus, Dr. Rainer, Cert. Chem.; 4000 Düsseldorf

27 03 185

45-775

4000 Düsseldorf 13, 1/24/1977
Henkelstraße 67

Henkel & Co. GmbH
Patent Department
Z/Pm.

Patent Application

D.5539

Cosmetic Agents Containing Skin Moisturizers

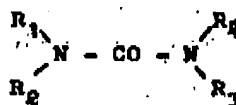
The present invention pertains to cosmetic agents, especially skin care, skin protective and skin-cleansing agents containing hydroxyalkyl-substituted ureas as the skin moisturizer.

It has been generally known that the protective measures for a healthy skin include a certain hygroscopicity besides other factors. If the substances on which this hygroscopicity as well as its constant restoration is based are removed from the skin due to environmental effects and extracting substances, the effects of chemicals and intense weathering effects, changes will occur in the stratum corneum, by which the protective action of the skin against damaging environmental effects may be greatly reduced.

The object was therefore to develop cosmetic agents, especially skin care, skin protective and skin-cleansing agents, by which the ability of the skin to function is preserved fully or to an increased extent despite damaging environmental effects and the restoration of the stratum corneum is effectively supported in case of damage that has actually occurred.

The products used hitherto as skin moisturizers were consistently ionic compounds such as acids and primarily salts, which considerably reduce the stability of especially low-viscosity O/W emulsions, even though they led to useable results as skin moisture regulators in some cases. In many cases, only completely insufficient amounts of skin moisture regulators were often able to be used in such cases. Besides the general object of developing good skin moisturizers, there was a special interest in products that do not cause any stability problems after their incorporation in O/W emulsions as well.

This object was accomplished by using cosmetic agents, especially skin care, skin protective and skin-cleansing agents based on usual components such as surfactants, emulsifying agents, fat substances, plant extracts, solvents, perfumes, thickeners and preservatives which contain hydroxyalkyl-substituted ureas according to the general formula



in which R_1 , R_2 , R_3 and R_4 denote, independently from one another, a hydrogen atom, a lower (C_1 - C_4) alkyl or a lower (C_2 - C_4) hydroxyalkyl group, which may contain 1-5 hydroxyl or hydroxyalkyl groups, providing that at least one of the radicals R_1 - R_4 is a hydroxyalkyl or

27 03 185

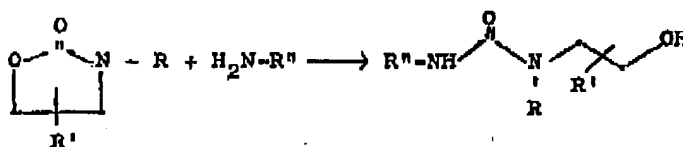
45-715

oligohydroxyalkyl group, in an amount of 1 wt. % to 20 wt. % and preferably 3 wt. % to 10 wt. % relative to the total agent.

These products, to be used according to the present invention, are especially suitable for maintaining or restoring the water retention of the skin and for keeping the skin soft and flexible and fully able to function as a result.

The compounds to be used as skin moisturizers according to the present invention can be prepared according to generally known methods. For example, they can be obtained by reacting substituted primary or secondary amines with urea at elevated temperatures of about 80°C to 200°C or by reacting the substituted amine hydrochlorides with alkali cyanates in an aqueous medium. Reactions of carbamic acid, which may be substituted at the nitrogen atom, with optionally substituted primary or secondary amines also yield the corresponding hydroxyalkyl-substituted ureas. The hydroxyalkyl-substituted ureas to be used according to the present invention may also be prepared by a reaction with isocyanates, carbamoyl chlorides or phosgene from correspondingly substituted amines.

It was furthermore found that *N*-(2-hydroxyalkyl) ureas can be prepared in a simple manner by allowing optionally substituted 2-oxazolidones to react with primary or secondary, especially primary amines at elevated temperature between preferably 100°C and 200°C. The reaction takes place according to the following scheme:



Hydroxyalkyl-substituted ureas to be used according to the present invention are, e.g., *N*-(2-hydroxyethyl), *N*-(2-hydroxypropyl), *N*-(3-hydroxypropyl), *N*-(2,3-dihydroxypropyl), *N*-(2,3,4,5,6-pentahydroxyhexyl), *N*-methyl-*N*-(1,3,4,5,6-pentahydroxy-2-hexyl), *N*-methyl-*N'*-(1-hydroxy-2-methyl-2-propyl), *N*-(1-hydroxy-2-methyl-2-propyl), *N*-(1,3-dihydroxy-2-propyl), *N*-(tris-hydroxymethyl-methyl), *N*-ethyl-*N'*-(2-hydroxyethyl), *N,N*-bis-(2-hydroxyethyl), *N,N'*-bis-(2-hydroxyethyl), *N,N*-bis-(2-hydroxypropyl), *N,N'*-bis-(2-hydroxypropyl), *N,N*-bis-(2-hydroxyethyl)-*N'*-propyl, *N,N*-bis-(2-hydroxypropyl)-*N'*-(2-hydroxyethyl), *N*-*tert*.-butyl-*N'*-(2-hydroxyethyl)-*N'*-(2-hydroxypropyl), *N*-(1,3-dihydroxy-2-propyl)-*N'*-(2-hydroxyethyl), *N,N*-bis-(2-hydroxyethyl)-*N'*,*N'*-dimethyl, *N,N,N',N'*-tetrakis-(2-hydroxyethyl)-*N'*,*N'*-dimethyl, *N,N,N',N'*-tetrakis-(2-hydroxyethyl), and *N,N*-bis-(2-hydroxyethyl)-*N'*,*N'*-bis-(2-hydroxypropyl) ureas.

The hydroxyalkyl-substituted ureas to be used according to the present invention are colorless, crystalline or viscous, fully stable products, which have very good physiological tolerance and are characterized as neutral, nonionic compounds by an especially good ability to be incorporated in cosmetic emulsion bases. Mixtures of various hydroxyalkyl-substituted ureas as well as mixtures with unsubstituted ureas may also be used for the incorporation in cosmetic products. Furthermore, it is not absolutely necessary to prepare the pure compounds, but the crude products of the reaction may also be used if they are adjusted to a neutral pH value by treatment with an acid cation exchanger.

27 03 199

45-775

Day creams, baby lotions, night creams and makeup creams, cleansing creams, skin protective creams, glycolic creams, creams with special additives of animal and vegetable origin, sunscreen creams and sunscreen emulsions, soaps, bath oils, steam baths, shower baths, face lotions, and aftershave may be mentioned as skin care, skin protective and skin-cleansing agents to which special skin care properties are imparted due to the addition of the *N*-hydroxyalkyl succinic acid amides to be used according to the present invention. The incorporation in the skin care, skin protective and skin-cleansing agents may be carried out in the known manner by simple stirring in or dissolution. Besides the hydroxyalkyl-substituted ureas to be used according to the present invention, the cosmetic preparations may contain the components usually present in such preparations, e.g., emulsifying agents, fat substances, plant extracts, preservatives, perfumes, and solvents in the usual quantities. The pH value of the skin care and skin protective agents may be in the acid to neutral range and is advantageously adjusted to weakly acid values around pH 6. The weakest possible alkaline pH is desirable in the case of soap-based skin-cleansing agents.

The subject of the present invention will be explained in greater detail by the following examples, but the subject of the present invention is not limited to these examples.

EXAMPLES

The compounds listed below were subjected to corresponding tests among the hydroxyalkyl-substituted ureas to be used according to the present invention as skin moisturizers, and they were used in formulations. The preparation of the products will be described first.

A) *N*-C₂-Hydroxyethyl Urea

A mixture of 61 g (1 mole) of ethanediolamine and 50 g (1 mole) of urea were heated for 8 hours at 100°C. The mixture crystallized after cooling, and *N*-(2-hydroxyethyl) urea with a melting point of 80-81°C was obtained at a nearly quantitative yield. It was possible to raise the melting point to 90-93°C by recrystallization from ethanol/ether.

However, purification by recrystallization is not necessary for use in the production of cosmetic products. The aqueous solution of the crude product is mixed for this purpose with the H form of a cation exchange resin, e.g., Lewatit S 100[®], while stirring, until a pH value of 6 becomes established, and subsequently filtered off. The aqueous solution of the *N*-(2-hydroxyethyl) urea thus obtained can be used for cosmetic purposes without any further treatment.

The following compounds were prepared in a corresponding manner:

B) *N*-C₃-Hydroxypropyl Urea

Melting point 118°C after recrystallization from dioxane.

C) *N,N*-Bis-C₂-Hydroxyethyl Urea

Melting point 75-76°C after recrystallization from chloroform/ethanol.

27 43 185

45-775

D) N-(2-Hydroxyethyl-2-methyl-2-propyl) Urea

A solution of 81 g (1 mole) of 2-amino-2-methyl propanol in 100 mL of water was neutralized with 100 g of 36% hydrochloric acid (1 mole) and subsequently mixed with a suspension of 65 g (1 mole) of sodium cyanate in 300 mL of water, which was added in portions, while stirring at room temperature. After stirring for 16 hours at room temperature, the solution was concentrated by evaporation under reduced pressure, and the solid residue was extracted with boiling ethanol. After the ethanol had been distilled off, the residue was recrystallized from ethanol. Thirty-six g of pure *N*-(2-hydroxy-2-methyl-2-propyl) urea with a melting point of 104°C, corresponding to 27% of the theoretical value, were obtained.

The following compounds were prepared in a corresponding manner:

E) N-(1,3-Dihydroxy-2-methyl-2-propyl) Urea

Colorless resin with a refractive index n^{20} of 1.5030.

F) N-(1,3-Dihydroxy-2-hydroxymethyl-2-propyl) Urea

Melting point 138°C after recrystallization from ethanol.

G) N,N'-Bis-(2-hydroxyethyl) Urea

A mixture of 43.5 g (0.5 moles) of 2-oxazolidone and 30.6 g (0.5 moles) of ethanalamine were heated at 145°C for 2 hours. After cooling with ice/water, the crude *N,N'*-bis-(2-hydroxyethyl) urea solidified into a wax-like mass. After recrystallization from ethanol/chloroform, the pure compound had a melting point of 54-55°C.

The products C, D, E, and F are novel compounds not hitherto described as such.

The favorable behavior of the compounds to be used according to the present invention in terms of water absorption capacity and water retention capacity was determined by means of the testing methods described in detail below. This is a method for determining the equilibrium moisture content, which is an indicator of the water retention capacity, and the determination of the water retention, rehydration and elasticity of impregnated porcine epidermis.

1. Determination of the Equilibrium Moisture Content

The substances to be tested (approx. 300-500 mg) were moistened with a defined quantity of water and exposed to different relative humidity levels (1%, 30%, 47%, 65%, 89% and 100% of relative humidity) at 23°C for 24 hours in a closed space. The amount of water taken up or removed was determined gravimetrically and plotted graphically. The relative humidity at which neither the release of water nor water uptake takes place was determined from the resulting curves. This value, which is called the equilibrium moisture content, is an indicator of the water retention capacity of a substance. The lower the value, the more favorably can the substance be rated. Furthermore, the water uptake capacity (hygroscopicity) of the substance can be read from the slope of the curve.

27 03 185

45-775

2. Measurements on Porcine Epidermis**a) Obtaining of the Porcine Epidermis**

Immediately after the pigs were sacrificed, the bristles of the skin were cut off by means of a hair-clipping machine (clipping head 0.1 mm). The pigs were blanchd in water with a temperature of 60°C for about 3-5 minutes, the epidermis was subsequently peeled off and stored at -20°C until use.

b) Determination of the Water Retention and the Rehydration of Impregnated Porcine Epidermis

Punched-out pieces of epidermis (1 x 2 cm) were soaked in a 10% solution of the substance to be tested for 2 hours, dabbed off under standardized conditions by means of a small press and dried for 24 hours, hanging freely between two clamps in a 100-mL Erlenmeyer flask at 23°C and a relative humidity of 30% as well as at 50% relative humidity (set by means of sulfuric acid-water mixtures). The drying of the impregnated sample to X % of the initial weight was compared with the corresponding value of the epidermis that was soaked in water only (blank value). The improvements in the water retention as well as in the rehydration compared with the blank value in Δ % H₂O are shown in the table. The deviations were at most ± 2 absolute units in the double tests. The test was repeated in the case of greater deviations. The rehydration was determined analogously by 24-hour drying of the impregnated and dabbed-off porcine epidermis at

30% relative humidity and subsequent incubation for 24 hours at
90% relative humidity.

c) Elasticity Measurements on Impregnated Porcine Epidermis

Punched-out pieces of epidermis (1 x 6 cm) were soaked in a 10% aqueous solution of the substance to be tested for 2 hours and dabbed off under standardized conditions. The samples were incubated hanging freely between two clamps at a relative humidity of 70% and at a relative humidity of 90% for 24 hours and stretched in a Zwick tensile testing machine (model 1402) under a load of 0-50 p. The stretching in mm, which was measured in the Hookean range at a load between 5 and 30 p, was stated as the indicator of the elasticity.

The measured values obtained in the above-described tests are shown in Table 1 below.

27 03 185

45-775

Table 1

Product	Equilibrium moisture content (% rel. hum.)	Measurements on the porcine epidermis				
		Water retention, % H ₂ O after drying at		Rehydration, % of water uptake at 90% rel. hum.	Stretching in mm after loading between 5 and 30 g	
		30% rel. hum.	50% rel. hum.		90% rel. hum.	75% rel. hum.
Blank value	-	0	0	0	0.3-0.5	0
A	70	15	18	21	6.2	0.8
C	62	10	10	11	5.1	1.5
G	58	11	11	15	4.7	0.8

The table above also shows the considerable water retention capacity of the compounds to be used according to the present invention and consequently their good suitability for use as skin moisturizers in skin care, skin protective and skin-cleansing agents, besides the high water uptake capacity.

Some examples of cosmetic preparations that contain the substances to be used according to the present invention as skin moisturizers will be described below.

Day Cream, Slightly Greasy

Fatty acid partial glyceride Cutina MD®

Dehydag

Stearic acid

Mixture of nonionogenic emulsifying agents

Eumulgin C 700® Dehydag

2-Octyl dodecanol

Vegetable oil

Paraffin oil

Triethanolamine

1,2-Propylene glycol

Product A

Nipagin M

Perfume oil

Water

6.0 parts by weight

8.0 parts by weight

3.0 parts by weight

4.0 parts by weight

3.0 parts by weight

5.0 parts by weight

0.4 parts by weight

3.0 parts by weight

6.0 parts by weight

0.2 parts by weight

1.0 part by weight

60.4 parts by weight

27 03 185

45-775

Baby Cream

Mixture of higher-boiling esters, predominantly mixed esters of pentaerythritol fatty acid esters and citric acid fatty alcohol esters, Dehymuls E® Dehydag

Oleic acid decyl ester

Vaseline

Wool grease

Boric acid

Talc

Zinc oxide

Nipagin M

Product G

Water

7.0 parts by weight
10.0 parts by weight
10.0 parts by weight
5.0 parts by weight
0.2 parts by weight
12.0 parts by weight
8.0 parts by weight
0.2 parts by weight
8.0 parts by weight
39.6 parts by weight

Night Cream

Colloid-disperse mixture of 90 parts of cetyl stearyl alcohol and 10 parts of sodium lauryl sulfate

2-Octyl dodecanol

Vegetable oil

Wool grease

Glycerol

Product C

Nipagin M

Perfume oil

Water

10.0 parts by weight
12.0 parts by weight
7.0 parts by weight
2.0 parts by weight
1.0 parts by weight
10.0 parts by weight
0.2 parts by weight
1.0 parts by weight
56.8 parts by weight

Boron-Glycerol Cream

Colloid-disperse mixture of 90 parts of cetyl stearyl alcohol and 10 parts of sodium lauryl sulfate

2-Octyl dodecanol

Vegetable oil

Boric acid

Glycerol

Nipagin M

Product B

Water

12.0 parts by weight
8.0 parts by weight
5.0 parts by weight
2.0 parts by weight
28.0 parts by weight
0.2 parts by weight
6.0 parts by weight
38.8 parts by weight

Moisturizing Cream

Mixture of mono- and diglycerides of palmitic and stearic acids, Eumulsan MD® Dehydag

Fatty alcohol polyglycol ether,

Eumulgin B 3® Dehydag

Oleic acid decyl ester

Vegetable oil

Paraffin oil

Product A

1,2-Propylene glycol

p-Hydroxybenzoic acid methyl ester

Water

16.0 parts by weight
4.0 parts by weight
5.0 parts by weight
5.0 parts by weight
2.0 parts by weight
5.0 parts by weight
5.0 parts by weight
5.0 parts by weight
0.2 parts by weight
57.8 parts by weight

27 03 185

45-775

Moisturizing Cream

Self-emulsifying mixture of mono- and diglycerides of higher saturated fatty acids, Eumulsan KD® Dehydag

Fatty alcohol polyglycol ether

Eumulgin B 3® Dehydag

2-Octyl dodecanol

Isopropyl myristate

Paraffin oil

Product G

Sorbitol solution Karion®, liquid

p-Hydroxybenzoic acid methyl ester

Water

16.0 parts by weight

1.0 parts by weight

12.0 parts by weight

8.0 parts by weight

4.0 parts by weight

5.0 parts by weight

8.0 parts by weight

0.2 parts by weight

55.8 parts by weight

Moisturizing Emulsion

Mixture of mono- and diglycerides of palmitic and stearic acids, Eumulsan MD® Dehydag

Fatty alcohol polyglycol ether, Eumulgin B 3® Dehydag

2-Octyl dodecanol

Vegetable oil

Paraffin oil

Product B

1,2-Propylene glycol

p-Hydroxybenzoic acid methyl ester

Water

6.0 parts by weight

4.0 parts by weight

10.0 parts by weight

4.0 parts by weight

4.0 parts by weight

5.0 parts by weight

7.0 parts by weight

0.2 parts by weight

59.8 parts by weight

Sunscreen Cream

Mixture of higher-molecular-weight esters with fat substances,

Dehymuls K® Dehydag

Oleic acid decyl ester

Sunscreen

Nipagin M

Product D

Water

30.0 parts by weight

15.0 parts by weight

5.0 parts by weight

0.2 parts by weight

8.0 parts by weight

41.8 parts by weight

Face-pack

Mixture of fatty acid partial glyceride with emulsifying agents, Cutina LE® Dehydag

Oleic acid decyl ester

Vitamin oil

Kaolin

Rice starch

Nipagin M

Product F

Water

12.0 parts by weight

4.0 parts by weight

5.0 parts by weight

2.0 parts by weight

3.0 parts by weight

0.2 parts by weight

10.0 parts by weight

63.8 parts by weight

27 03 185

45-775

Syndet Soap Bar Containing Skin Moisturizer

The example is based on a syndet bar based on a mixture of olefin sulfonate and sulfosuccinic acid ester salt.

The disodium salt of a sulfosuccinic acid monofatty alcohol ester, which had been prepared from the C₁₂-C₁₈ fraction of a cocofatty alcohol, was used to prepare the mixture. The olefin sulfonate originated from a mixture of straight-chain α -olefins containing 15-18 carbon atoms. This olefin mixture was prepared by sulfonating 1 mole of olefin with approx. 1.2 moles of gaseous, inert gas-diluted sulfur trioxide, hydrolyzing the crude sulfonation product with the calculated amount of sodium hydroxide at temperatures of about 100°C and bleaching the sulfonate with hypochlorite. The mixture of the two sulfonates contained about 5 wt. % of neutral salt (sodium sulfate and sodium chloride) relative to anhydrous sulfonate. The composition of the syndet mass was as follows:

- 70 parts by weight of surfactant mixture, consisting of
 - 60 wt. % of olefin sulfonate
 - 40 wt. % of the disodium salt of the sulfosuccinic acid ester
- 15 parts by weight of tallow fatty acid (iodine number 2)
- 2 parts by weight of lanolin
- 5 parts by weight of water
- 8 parts by weight of product G
- 2 parts by weight of perfume oil.

The mass was molded in an extruder and pressed into bars.

Other products that can be used according to the present invention may also be used instead of the compounds to be used according to the present invention that are mentioned in the above formulations.